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09/485,005	09/11/2000	Erich Wanker	V0179/7001	1379

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 08/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/485,005	WANKER ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 6/17/04.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-26 is/are pending in the application.

4a) Of the above claim(s) 21-26 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-12 and 17-20 is/are rejected.

7)☒ Claim(s) 13-16 is/are objected to.

8)☒ Claim(s) 1-26 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment filed 6/17/04 is acknowledged and has been entered. Claims 21-26 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Claims 12 and 13 have been amended. Currently, claims 1-26 are pending. Claims 1-20 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 102

2. In light of Applicant's amendment and argument, the rejection of claims 1-12 and 17-20 under 35 U.S.C. 102(e) as being anticipated by Kalchman et al. (US 6,235,879), is hereby, withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 11 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 11 is vague and indefinite because it is unclear how detection is "effected by electron microscopy, ...". Specifically, it is unclear what Applicant intends to encompass in reciting, "effected" as used in the claim. Does Applicant intend, "detection ... is performed by electron microscopy, ...".

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 17 recites the broad recitation "at least 35", and the claim also recites "preferably at least 41, more preferably at least 48, and most preferably at least 41" which is the narrower statement of the range/limitation.

Claim 17 is also vague and indefinite in reciting, "preferably", "more preferably", and "most preferably" because they are subjective terms that lack a comparative basis for defining their metes and bounds.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 6-12, and 18-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Mignotte et al. (Mitochondrial DNA-Binding Proteins that bind preferentially to Supercoiled Molecules containing the D-Loop Region of Xenopus Laevis mtDNA, Biochemical and Biophysical Research Communications, November 30, 1983).

Mignotte et al. teaches a method of detecting the presence of detergent- or urea-insoluble amyloid-like fibrils or protein aggregates (fraction of proteins insoluble in 1% Triton-X 100 enriched in DNA-binding proteins or DBP) on a filter. The protein aggregates are from a cellular sample of an animal (Xenopus laevis). The fraction of proteins is detected by filter binding assay (see Abstract and page 99). In practice, Mignotte et al. contacts (pipets) protein aggregates previously treated with detergent or urea (reaction mixture) to solubilize the sample, filters the reaction mixture to capture the detergent- or urea-insoluble protein aggregates, washes the filter to remove detergent or urea soluble material of the sample from the reaction mixture, and detects or measures the protein aggregates retained on the filter that is bound to a tag (^{14}C label and ^{3}H label) using microscopy. Mignotte et al. teaches using SDS or TRITON X-

100 as detergent. Specifically, the reaction mixture is filtered or sucked through the filter membrane at a flow rate of 3 ml/min. Mignotte et al. uses cellulose acetate filter (nitrocellulose filter or DNA cellulose column) having a low capacity for protein adsorption to filter the reaction mixture (see page 100 and 101).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 2, 3, and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mignotte et al. (Mitochondrial DNA-Binding Proteins that bind preferentially to Supercoiled Molecules containing the D-Loop Region of Xenopus Laevis mtDNA, Biochemical and Biophysical Research Communications, November 30,1983) in view of Tateishi et al (Removal of Causative Agent of Creuzfeldt-Jacob Disease through membrane filtration method, Membrane, 1993).

Mignotte et al. has been discussed supra. Mignotte et al. differ from the claimed invention in failing to teach that the amyloid-like fibrils of protein aggregates are indicative of disease.

Tateishi et al. teach a method of detecting and removing detergent insoluble amyloid-like fibrils or protein aggregates (prion protein or PrPCJD) from the brain sample of mice with spongiform encephalopathy using a filter (virus removal membrane)

which is cuprammonium regenerated cellulose hollow fiber (see Abstract and page 358, column 1). The existence of detergent insoluble amyloid-like fibrils or protein aggregates is indicative of the neurodegenerative disease (agent infectivity) in humans (see page 361, column 2). The presence of PrPCJD protein is detected immunohistchemically using a chemical reagent (see page 359, column 2).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to capture and detect the protein aggregates indicative of human neurodegenerative disease in the teaching of Tateishi using the method as taught by Mignotte wherein protein aggregates retained on the filter are detected and measured using microscopy because both Tateishi and Mignotte teach methods to achieve isolation and detection of detergent- or urea- insoluble protein aggregates using a filter membrane and the protein aggregate forms taught by Tateishi and Mignotte are obvious variations of protein aggregates that are known to be insoluble to Triton-X 100 detergent.

6. Claims 4 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mignotte et al. (Biochemical and Biophysical Research Communications, November 30,1983) in view of Tateishi et al (Membrane, 1993) and in further view of Stott et al. (Proc. Natl. Acad. Sci. USA, 1995).

Mignotte et al. and Tateishi et al. have been discussed supra. has been discussed supra. Mignotte et al. and Tateishi et al. differ from the claimed invention in

failing to teach that the diseases upon which the protein aggregates are indicative of, is associated with polyglutamine expansion.

Stott et al. teach that some proteins contain polyglutamine repeats and their abnormal expansion is linked to neurodegenerative diseases. Stott et al. teach that polyglutamine forms B-strands which are held together by hydrogen bonds between their amide groups, thus, forming polar zippers. Multiplicity of hydrogen bonds between extended strands of glutamine repeats in an oligomer increases stability of these proteins (see page 6509). Stott et al. teach that pathological effects and abberant transcriptional activity arise when expanded glutamine repeats cause proteins to acquire excessively high affinities for each other or for complementary regulatory proteins with glutamine repeats (see page 6512).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the teaching of Stott that proteins having polyglutamine expansion such as those linked to neurodegenerative disease have excessively high affinities to each other, into the method of Mignotte as modified by Tateishi, for applications in protein aggregate isolation and detection because both Tateishi and Mignotte teach methods to achieve isolation and detection of proteins with excessively high affinities for each other such as those that are detergent- or urea-insoluble including those that are associated with polyglutamine expansion in the teaching of Stott.

Allowable Subject Matter

7. Claims 13-16 would be allowable if rewritten to overcome the rejections under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

Claims 13-16 are clear of the prior art of record. The prior art of record fails to teach or fairly suggest a fusion protein for use in the method of claim 1, comprising 1) a (poly)peptide that enhances solubility or prevents aggregation of the fusion protein; 2) an amyloidogenic (poly)peptide [that self assembles into amyloid-like fibrils or protein aggregates when released from the fusion protein]; and 3) a cleavable site that separates 1) and 2) of the fusion protein; and wherein the fusion protein is further incubated with a suspected inhibitor of amyloid-like fibrils and protein aggregate formation, and simultaneously or concurrently, with a compound that induces cleavage at the cleavage site.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703) 305-0807. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (703) 305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-0169.

Gailene R. Gabel
Patent Examiner
Art Unit 1641
August 17, 2004

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
8/17/04